Complete Summary

GUIDELINE TITLE

Depression. A guide to diagnosis and treatment.

BIBLIOGRAPHIC SOURCE(S)

Brigham and Women's Hospital. Depression. A guide to diagnosis and treatment. Boston (MA): Brigham and Women's Hospital; 2001. 9 p. [6 references]

GUIDELINE STATUS

This is the current release of the guideline.

* * REGULATORY ALERT * *

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- On May 12, 2006, GlaxoSmithKline (GSK) and the U.S. Food and Drug Administration (FDA) notified healthcare professionals of changes to the Clinical Worsening and Suicide Risk subsection of the WARNINGS section in the prescribing Information for Paxil and Paxil CR. These labeling changes relate to adult patients, particularly those who are younger adults.

  A recent meta-analysis conducted of suicidal behavior and ideation in placebo-controlled clinical trials of paroxetine in adult patients with psychiatric disorders including Major Depressive Disorder (MDD), other depression and non-depression disorders. Results of this analysis showed a higher frequency of suicidal behavior in young adults treated with paroxetine compared with placebo. Further, in the analysis of adults with MDD (all ages), the frequency of suicidal behavior was higher in patients treated with paroxetine compared with placebo. This difference was statistically significant; however, as the absolute number and incidence of events are small, these data should be interpreted with caution. All of the reported events of suicidal behavior in the adult patients with MDD were non-fatal suicide attempts, and the majority of these attempts (8 of 11) were in younger adults aged 18-30. These MDD data suggest that the higher frequency observed in the younger adult population across psychiatric disorders may extend beyond the age of 24.

  It is important that all patients, especially young adults and those who are improving, receive careful monitoring during paroxetine therapy regardless of the condition being treated. See the FDA Web site for more information.

- On December 8, 2005, the U.S. Food and Drug Administration (FDA) has determined that exposure to paroxetine in the first trimester of pregnancy may increase the risk for congenital malformations, particularly cardiac malformations. At the FDA's request, the manufacturer has changed paroxetine's pregnancy category from C to D and added new data and recommendations to the WARNINGS section of paroxetine's prescribing information. FDA is awaiting the final results of the recent studies and accruing additional data related to the use of paroxetine in pregnancy in order to better characterize the risk for congenital malformations associated with paroxetine.

  Physicians who are caring for women receiving paroxetine should alert them to the potential risk to the fetus if they plan to become pregnant or are currently in their first trimester of pregnancy. Discontinuing paroxetine therapy should be considered for these patients. Women who are pregnant, or planning a pregnancy, and currently taking paroxetine should consult with their physician about whether to continue taking it. Women should not stop the drug without discussing the best way to do that with their physician. See the FDA Web site for more information.

- On September 27, 2005, GlaxoSmithKline (GSK) and the U.S. Food and Drug Administration (FDA) notified healthcare professionals of changes to the Pregnancy/PRECAUTIONS section of the Prescribing Information for Paxil and Paxil CR Controlled-Release Tablets to describe the results of a GSK retrospective epidemiologic study of major congenital malformations in infants born to women taking antidepressants during the first trimester of pregnancy. This study suggested an increase in the risk of overall major congenital malformations for paroxetine as compared to other antidepressants [OR 2.2; 95% confidence interval, 1.34-3.63]. Healthcare professionals are advised to carefully weigh the potential risks and benefits of using paroxetine therapy in women during pregnancy and to discuss these findings as well as treatment alternatives with their patients. See the FDA Web site for more information.
- On July 1, 2005, in response to recent scientific publications that report the possibility of increased risk of suicidal behavior in adults treated with antidepressants, the U.S. Food and Drug Administration (FDA) issued a Public Health Advisory to update patients and healthcare providers with the latest information on this subject. Even before the publication of these recent reports, FDA had already begun the process of reviewing available data to determine whether there is an increased risk of suicidal behavior in adults taking antidepressants. The Agency has asked manufacturers to provide information from their trials using an approach similar to that used in the evaluation of the risk of suicidal behavior in the pediatric population taking antidepressants. This effort will involve hundreds of clinical trials and may take more than a year to complete. See the FDA Web site for more information.

COMPLETE SUMMARY CONTENT

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SCOPE

DISEASE/CONDITION(S)

Depression, including depressive disorders unique to women, such as premenstrual dysphoric disorder (PMDD), postpartum depression, and depression during menopause

GUIDELINE CATEGORY

Diagnosis
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Obstetrics and Gynecology
Psychiatry
Psychology

INTENDED USERS

Advanced Practice Nurses
Health Care Providers
Physician Assistants
Physicians
Psychologists/Non-physician Behavioral Health Clinicians
Social Workers

GUIDELINE OBJECTIVE(S)

To assist the primary care physician (PCP) in identifying patients in need of treatment and how to optimally treat them

TARGET POPULATION

Women

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis

1. Diagnostic strategy using criteria listed in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)
2. Use of SIGECAPS (mnemonic system for diagnosis of depression)
3. Measurement of thyroid stimulating hormone in perimenopausal women

Treatment/Management

1. Psychotherapy
2. Pharmacotherapy
    - Tricyclic antidepressants, such as nortriptyline (Pamelor, Aventyl); desipramine (Norpramine), clomipramine (Anafranil)
    - Monoamine oxidase inhibitors (MAOIs), such as phenelzine (Nardil), tranylcypromine (Parnate)
    - Selective serotonin reuptake inhibitors (SSRIs), such as fluoxetine (Prozac, Prozac Weekly, Sarafem); sertraline (Zoloft); paroxetine (Paxil); fluvoxamine (Luvox); citalopram (Celexa)
    - Other antidepressants, such as trazodone (Desyrel), bupropion (Wellbutrin, Wellbutrin SR, Zyban), venlafaxine (Effexor and Effexor XR), mirtazapine (Remeron), nefazodone (Serzone)
3. Adjunctive therapy, such as anxiolytics
4. Referral to psychiatry, substance abuse clinic, or emergency department, as needed

MAJOR OUTCOMES CONSIDERED

- Risk of morbidity and mortality both through suicide as well as comorbid medical disorders
- Prevalence rate of depression in women
- Recurrence rate and risk of recurrence of depression
- Symptoms of depression
- Side effects of medications to treat depression

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The guideline developer performed literature searches using Medline.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Subjective Review

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

This guideline was reviewed by the Women's Health Guidelines Editorial Review Board.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Diagnostic Strategy

Depression does not always present as sadness. It can also be characterized by somatic symptoms or at times physical symptoms with no clear-cut organic basis. Similarly, not all sadness is depression. A definitive diagnosis of depression requires satisfying criteria listed in the Diagnostic and Statistical Manual of Mental

Disorders (DSM-IV). To make the diagnosis of major depression or dysthymia use SIGECAPS, a mnemonic system which is a concise version of the DSM-IV criteria. Both disorders require active treatment.

Major depression = depressed mood or interest + 4 SIGECAPS for 2 or more weeks

Dysthymia = depressed mood or interest + 3 SIGECAPS most days for 2 or more years

Sleep increase/decrease
Interest in formerly compelling or pleasurable activities diminished
Guilt, low self esteem
Energy poor
Concentration poor
Appetite increase/decrease
Psychomotor agitation or retardation
Suicidal ideation

Treatment

The Depression Management Algorithm may be referred to (see page 5 in the original guideline document). Psychotherapy may be as effective as medication in the treatment of mild to moderate depression, and should be considered especially in patients who would prefer to avoid medications. If there is no improvement after six to eight weeks of therapy, or if there is not complete resolution by 12 weeks, antidepressant medications are recommended. Since selective serotonin reuptake inhibitors (SSRIs) are associated with fewer medically significant side-effects compared with tricyclic antidepressants (TCAs) or monoamine oxidase inhibitor (MAOIs), they should be used as the first line of therapy. When selecting the specific SSRI to prescribe, comorbid conditions, age of the patient, prior history of response and family history of response should be taken into consideration.

When patients do not respond to treatment, the most common cause is non-compliance with medication. A second important cause of treatment failure is inadequate dosing or duration of therapy. Patients should always be started on the lowest dose of a medication to ensure that they can tolerate the medication. However, the dose should be advanced aggressively, if appropriate, with increases up to every one to two weeks as long as side effects are well-tolerated. Frequent visits (every one to two weeks) to monitor response at the beginning of therapy will minimize drop-out rates, since most side effects usually occur in the first few weeks of treatment. Some patients develop agitation early in the course of treatment. Often, a change to a different SSRI is well tolerated. If there is no response to treatment by 4 weeks, or if there is a less than 50% response by 8 weeks, the clinician should either change to a different agent and/or consider referral to a psychopharmacologist.

If the patient responds well to treatment, therapy should be continued for a total of 9 to 12 months from the time of initiation to prevent recurrence. For patients who have had 3 previous episodes of depression, or 2 episodes with risk factors, maintenance therapy is recommended. (See "Major Risk Factors for Recurrent

Depression" below.) Once patients have achieved remission and are on maintenance therapy, the medication should be continued.

Some patients with depression may have comorbid psychiatric symptoms. Patients with mild to moderate anxiety may require adjunctive therapy with anxiolytics (e.g., lorazepam, clonazepam) especially in the early stages of treatment. The goal of such treatment is to control symptoms such as sleeplessness and restlessness. Patients with coexistent substance abuse disorders, eating disorders, post traumatic stress or abuse disorders, obsessive compulsive disorders, or personality disorders may benefit from referral to psychiatric specialists. Patients who exhibit severe anxiety or anorexia, significant psychomotor agitation or retardation, psychosis or mania, and/or suicidal or homicidal thinking should be referred immediately to psychiatry.

Major Risk Factors for Recurrent Depression

The presence of any of the following should direct the primary care physician (PCP) to strongly consider maintenance use of antidepressants and/or a consultation with a psychiatrist:

- A family history of recurrent depression
- Family history of bipolar disorder
- Personal history of recurrence within one year after discontinuing effective treatment
- Onset of major depressive episode before age 20
- Severe, sudden, or life-threatening depressive episode (i.e., suicidal attempt)

Depressive Disorders Unique to Women

Because the gender specific aspects of depression have received little attention until recently, there are relatively few data on the depressive conditions associated with hormonal changes. Although there are few large randomized controlled trials for guidance, smaller, short-term studies and clinical experience have suggested approaches that may be helpful in relieving symptoms of the following:

Premenstrual Dysphoric Disorder (PMDD)

To satisfy the diagnostic criteria proposed in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), a woman should have at least five of the following symptoms, including at least one of the first four. Symptoms should occur during the last week of the luteal phase, resolve with the onset of menses, and have been present for at least two menstrual cycles.

- Depressed mood
- Marked anxiety or tension
- Mood swings
- Persistent anger or irritability
- Lack of interest in usual activities
- Difficulty concentrating
- Fatigue

- Increased appetite or food cravings
- Sleep disturbances
- Sense of being overwhelmed, physical symptoms (breast tenderness, bloating, weight gain, headache, joint pain)

The selective serotonin reuptake inhibitors (SSRIs) are the medications recommended for use in treatment of PMDD. Zoloft (Sertraline) was the first drug to show efficacy and recently the Food and Drug Administration (FDA) has approved Sarafem (which is fluoxetine or Prozac) for treating this disorder, though any SSRI is likely to benefit. While some clinicians have used these medications only during the luteal phase, most now recommend taking the medications daily, throughout the cycle.

When women are over 40, the symptoms of PMDD may overlap with those of perimenopause, and assessment of reproductive hormone levels may be helpful.

Postpartum Depression

One in ten women have a major depressive episode within four to 16 weeks after childbirth. The risk of postpartum depression (PPD) is approximately 25% in women who have a previous history of depression, up to 50% in those with a history of postpartum depression, and may be 75% in those who have been depressed during an on-going pregnancy. More than one episode of PPD increases the risk during each successive pregnancy.

The few physiologic studies to date of psychopharmacologic treatment for PPD have indicated that concentrations of antidepressants (SSRIs or tricyclics) in breast milk or the serum of breast-fed infants are very low or undetectable. The majority of reports suggest minimal risk of toxicity in infants. SSRIs are generally considered the first line of treatment for PPD, especially in women who are not breast-feeding or for women with moderate to severe depression. For those patients who are breastfeeding and who have mild to moderate depression, a careful risk benefit discussion must be done when prescribing, taking the above data into consideration. Psychosocial interventions (i.e., household support, couples counseling, and psychotherapy) are useful adjuncts to therapy. Finally, women with severe PPD, who verbalize thoughts about self harm or harm to the baby must be referred immediately and treated aggressively, often with a combination of antidepressants, antipsychotics, and hospitalization.

Depression During Perimenopause

There is increasing evidence that perimenopause--the period of transition from regular menstruation to cessation of menses--is associated with increased risk of depression and/or mood changes. It is also associated with dramatic and unpredictable variations in reproductive hormones. Because hypothyroidism occurs in 7 to 8% of women and increases in frequency with age, measurement of thyroid stimulating hormone is especially recommended for women in this age group who have signs of depression. Women with mild depression may benefit from hormone therapy, psychotherapy, and medications, like SSRIs. The SSRIs, are considered first line treatment for perimenopausal women with more significant depression and for those with a history of depression, although both groups may also benefit from hormone replacement therapy/estrogen

replacement therapy (HRT/ERT). Oral contraceptives are also often used as hormonal treatment prior to the complete cessation of menses.

CLINICAL ALGORITHM(S)

An algorithm is provided in the original guideline document for depression management.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Guideline recommendations are based on a comprehensive assessment of research on depression and the American Psychiatric Association´s Practice Guideline for Major Depressive Disorder in Adults.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Overall Benefits

- Improved diagnosis and treatment of depression in women
- Optimal, personalized care of depression in women

Specific Benefits of Commonly Used Antidepressants

- Tricyclic antidepressants (TCAs). Food and Drug Administration (FDA) approved for depression, no concerning risks yet evident during pregnancy or breastfeeding.
- Monoamine oxidase inhibitors (MAOIs). FDA approved for depression, very effective for atypical depression and anxiety disorders, may cause less rapid-cycling/mixed states than TCAs.
- Selective serotonin reuptake inhibitors (SSRIs). Less rapid-cycling/mixed states than TCAs, safe in overdose, no cardiotoxicity.

Additional benefits for specific drugs within each of the drug classes mentioned above may be found in the original guideline document.

The benefits of other commonly prescribed antidepressants, such as trazodone, bupropion, venlafaxine, mirtazapine, and nefazodone are itemized in the original guideline document.

Subgroups Most Likely to Benefit:

- Women with premenstrual dysphoric disorder
- Women with postpartum depression
- Women with perimenopause depression

POTENTIAL HARMS

Side Effects of Commonly Used Antidepressants

- Tricyclic antidepressants (TCAs). Weight gain, electrocardiographic (EKG) monitoring required, lethal in overdose, induction of rapid-cycling/mixed states.
- Monoamine oxidase inhibitors (MAOIs). Dietary and drug restrictions, overdose lethal, blood levels not helpful.
- Selective serotonin reuptake inhibitors (SSRIs). May be agitating or cause akathisia, sexual side-effects, may cause mild weight gain, cognitive "fuzz."

Additional harms for specific drugs within each of the drug classes mentioned above may be found in the original guideline document.

The harms of other commonly prescribed antidepressants, such as trazodone, bupropion, venlafaxine, mirtazapine, and nefazodone are itemized in the original guideline document.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This guide is not intended to convey rigid standards, but instead, provide the primary care physician an algorithm for thinking through the identification and management of depressed individuals. Treatment should be tailored to the needs of the individual woman.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm
Patient Resources

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Brigham and Women's Hospital. Depression. A guide to diagnosis and treatment. Boston (MA): Brigham and Women's Hospital; 2001. 9 p. [6 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2001

GUIDELINE DEVELOPER(S)

Brigham and Women's Hospital (Boston) - Hospital/Medical Center

SOURCE(S) OF FUNDING

Funding was provided by Brigham and Women's Hospital.

GUIDELINE COMMITTEE

Not stated

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Depression Guideline Authors: Randy Glassman, MD; Lori Farnan, MD; Soheyla Gharib, MD; Jane Erb, MD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the Brigham and Women's Hospital Web site.

Print copies: Available from the Brigham and Women's Hospital, 75 Francis Street, Boston, MA 02115; telephone: (800) BWH-9999; Web site: www.brighamandwomens.org.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

The following is available:

- Depression. Taking care of your emotional health. Boston (MA): Brigham and Women's Hospital. 2002 Nov. 12 p.

Electronic copies: Available in Portable Document Format (PDF) from the Brigham and Women's Hospital Web site.

Print copies: Available from the Brigham and Women's Hospital, 75 Francis Street, Boston, MA 02115; telephone: (800) BWH-9999; Web site: www.brighamandwomens.org.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This summary was completed by ECRI on January 28, 2003. The information was verified by the guideline developer on February 10, 2003. This summary was updated by ECRI on August 15, 2005, following the U.S. Food and Drug Administration advisory on antidepressant medications. This summary was updated by ECRI on October 3, 2005, following the U.S. Food and Drug Administration advisory on Paxil (paroxetine). This summary was updated by ECRI on December 12, 2005, following the U.S. Food and Drug Administration advisory on Paroxetine HCL - Paxil and generic paroxetine. This summary was updated by ECRI on May 31, 2006 following the U.S. Food and Drug Administration advisory on Paxil (paroxetine hydrochloride).

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